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Term	Documents
IKB.USPT.	54
IKBS	0
W.USPT.	647022
WS.USPT.	5806
ALPHA.USPT.	261237
ALPHAS.USPT.	237
KINASE.USPT.	13289
KINASES.USPT.	2866
((IKB ADJ W ADJ ALPHA) AND KINASE).USPT.	0

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Refine Search: ikb(w)alpha and kinase Clear

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Today's Date: 5/23/2000

DB Name	Query	Hit Count	Set Name
USPT	ikb(w)alpha and kinase	0	L4
JPAB,EPAB,DWPI	ikb(w)alpha and kinase	0	L3
JPAB,EPAB,DWPI	ikk(w)gamma	0	L2
USPT	ikk(w)gamma	0	L1

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? s ikk(w)gamma

          208  IKK
       351270  GAMMA
S1         10  IKK(W)GAMMA
? rd

...completed examining records
S2          7  RD (unique items)
? t s2/3,ab/all


 2/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10339346   20190098
  Somatic mutagenesis studies of NF-kappa B signaling in human T cells:
evidence for an essential role of IKK gamma in NF-kappa B
activation by T-cell costimulatory signals and HTLV-I Tax protein.
  Harhaj EW; Good L; Xiao G; Uhlik M; Cvijic ME; Rivera-Walsh I; Sun SC
  Department of Microbiology and Immunology, Pennsylvania State University
College of Medicine, 500 University Drive, Hershey, Pennsylvania, PA 17033,
USA.
  Oncogene (ENGLAND)  Mar 9 2000,  19 (11) p1448-56,  ISSN 0950-9232
Journal Code: ONC
  Contract/Grant No.: R01CA68471, CA, NCI
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
  NF-kappa B plays a pivotal role in normal T-cell activation and may also
mediate human T-cell leukemia virus (HTLV)-induced T-cell transformation.
Activation of NF-kappa B by both T-cell costimulatory signals and the HTLV
Tax protein involves stimulation of I kappa B kinase (IKK). As a genetic
approach to dissect the intermediate steps involved in NF-kappa B
activation in human T cells, we performed somatic cell mutagenesis to
isolate signaling-defective mutant Jurkat T-cell lines. One of the mutant
cell lines was shown to have a specific blockade in the IKK signaling
pathway but remained competent in the c-Jun N-terminal kinase and MAP
kinase pathways. Interestingly, this mutant cell line lacks expression of
IKK gamma , a non-catalytic component of the IKK complex.
Expression of exogenous IKK gamma in the mutant cells restored
NF-kappa B activation by both the T-cell costimulation agents and Tax.
These findings provide genetic evidence for the requirement of IKK
gamma in NF-kappa B signaling triggered by both T-cell costimulatory
signals and HTLV-I Tax protein.


 2/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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10325366   20188876
  The I kappa B kinase (IKK) and NF-kappa B: key elements of
proinflammatory signalling.
  Karin M; Delhase M
  Department of Pharmacology, University of California San Diego, La Jolla
92093-0636, USA.
  Seminars in immunology (UNITED STATES)  Feb 2000,  12 (1) p85-98,  ISSN
```

1044-5323 Journal Code: A61
Contract/Grant No.: [redacted]04151, ES, NIEHS; AI43477, AI[redacted]AID; CA76188, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

NF-kappa B is a heterodimeric transcription factor that plays a key role in inflammatory and immune responses. In nonstimulated cells, NF-kappa B dimers are maintained in the cytoplasm through interaction with inhibitory proteins, the I kappa Bs. In response to cell stimulation, mainly by proinflammatory cytokines, a multisubunit protein kinase, the I kappa B kinase (IKK), is rapidly activated and phosphorylates two critical serines in the N-terminal regulatory domain of the I kappa Bs. Phosphorylated I kappa Bs are recognized by a specific E3 ubiquitin ligase complex and undergo polyubiquitination which targets them for rapid degradation by the 26S proteasome. NF-kappa B dimers, which are spared from degradation, translocate to the nucleus to activate gene transcription. There is strong biochemical and genetic evidence that the IKK complex, which consists of two catalytic subunits, IKK alpha and IKK beta, and a regulatory subunit, **IKK gamma** , is the master regulator of NF-kappa B-mediated innate immune and inflammatory responses. In the absence of **IKK gamma** , which normally connects IKK to upstream activators, no IKK or NF-kappa B activation can occur. Surprisingly, however, of the two catalytic subunits, only IKK beta is essential for NF-kappa B activation in response to proinflammatory stimuli. The second catalytic subunit, IKK alpha, plays a critical role in developmental processes, in particular formation and differentiation of the epidermis.

2/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10138543 99386936

Differential effects of lipopolysaccharide and tumor necrosis factor on monocytic IkappaB kinase signalsome activation and IkappaB proteolysis.

Fischer C; Page S; Weber M; Eisele T; Neumeier D; Brand K
Institute of Clinical Chemistry and Pathobiochemistry, Klinikumrechts der Isar, Technical University Munich, Ismaninger Strasse 22, 81675 Munich, Germany.

Journal of biological chemistry (UNITED STATES) Aug 27 1999, 274 (35) p24625-32, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The inflammatory mediators lipopolysaccharide (LPS) and tumor necrosis factor (TNF) are potent activators of NF-kappaB. This study compared the effect of these stimuli on endogenous IkappaB kinase (IKK) signalsome activation and IkappaB phosphorylation/proteolysis in human monocytic cells and investigated the role of the signalsome proteins IKK-alpha, IKK-beta, NF-kappaB-inducing kinase (NIK), **IKK-gamma** (NF-kappaB essential modulator), and IKK complex-associated protein. Kinase assays showed that TNF elicited a rapid but short-lived induction of IKK activity with a 3-fold greater effect on IKK-alpha than on IKK-beta, peaking at 5 min. In contrast, LPS predominantly stimulated IKK-beta activity, which slowly increased, peaking at 30 min. A second peak was observed at a later time point following LPS stimulation, which consisted of both IKK-alpha and -beta activity. The endogenous levels of the signalsome components were unaffected by stimulation. Furthermore, our studies showed association of the IKK-alpha/beta heterodimer with NIK, IkappaB-alpha and -epsilon in unstimulated cells. Exposure to LPS or TNF led to differential patterns of IkappaB-alpha and IkappaB-epsilon disappearance from and reassembly with the signalsome, whereas IKK-alpha, IKK-beta, and NIK remained complex-associated. NIK cannot phosphorylate IkappaB-alpha directly, but it appears to be a functionally important subunit, because mutated NIK inhibited stimulus-induced kappaB-dependent transcription more effectively than mutated IKK-alpha or -beta. Overexpression of IKK complex-associated

protein inhibited stimulus-mediated transcription, whereas NF-kappaB essential modulator enhanced it. The understanding of [redacted]- and TNF-induced signaling may allow the development of specific strategies to treat sepsis-associated disease.

2/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10133113 99292691
Role of adapter function in oncoprotein-mediated activation of NF-kappaB. Human T-cell leukemia virus type I Tax interacts directly with IkappaB kinase gamma.
Jin DY; Giordano V; Kibler KV; Nakano H; Jeang KT
Laboratory of Molecular Microbiology, NIAID, National Institutes of Health, Bethesda, Maryland 20892-0460, USA.
Journal of biological chemistry (UNITED STATES) Jun 18 1999, 274 (25) p17402-5, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Mechanisms by which the human T-cell leukemia virus type I Tax oncoprotein activates NF-kappaB remain incompletely understood. Although others have described an interaction between Tax and a holo-IkappaB kinase (IKK) complex, the exact details of protein-protein contact are not fully defined. Here we show that Tax binds to neither IKK-alpha nor IKK-beta but instead complexes directly with **IKK-gamma**, a newly characterized component of the IKK complex. This direct interaction with **IKK-gamma** correlates with Tax-induced IkappaB-alpha phosphorylation and NF-kappaB activation. Thus, our findings establish **IKK-gamma** as a key molecule for adapting an oncoprotein-specific signaling to IKK-alpha and IKK-beta.

2/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10113418 98421680
IKK-gamma is an essential regulatory subunit of the IkappaB kinase complex [see comments]
Rothwarf DM; Zandi E; Natoli G; Karin M
Department of Pharmacology, University of California San Diego, La Jolla 92093-0636, USA.
Nature (ENGLAND) Sep 17 1998, 395 (6699) p297-300, ISSN 0028-0836 Journal Code: NSC
Comment in Nature 1998 Sep 17;395(6699):225-6
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Pro-inflammatory cytokines activate the transcription factor NF-kappaB by stimulating the activity of a protein kinase that phosphorylates IkappaB, an inhibitor of NF-kappaB, at sites that trigger its ubiquitination and degradation. This results in the nuclear translocation of freed NF-kappaB dimers and the activation of transcription of target genes. Many of these target genes code for immunoregulatory proteins. A large, cytokine-responsive IkappaB kinase (IKK) complex has been purified and the genes encoding two of its subunits have been cloned. These subunits, IKK-alpha and IKK-beta, are protein kinases whose function is needed for NF-kappaB activation by pro-inflammatory stimuli. Here, by using a monoclonal antibody against IKK-alpha, we purify the IKK complex to homogeneity from human cell lines. We find that IKK is composed of similar amounts of IKK-alpha, IKK-beta and two other polypeptides, for which we obtained partial sequences. These polypeptides are differentially processed forms of a third subunit, **IKK-gamma**. Molecular cloning and sequencing indicate that **IKK-gamma** is composed of several

potential coiled-coil motifs. **IKK-gamma** interacts preferentially with IKK-beta and is required for the activation of the IKK complex. An **IKK-gamma** carboxy-terminal truncation mutant that still binds IKK-beta blocks the activation of IKK and NF-kappaB.

2/3,AB/6 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12329909 BIOSIS NO.: 200000083411
Differential expression of IkappaBalpha, IKKalpha, IKKbeta, and IKKgamma in various human cell lines and different tissues.
AUTHOR: Wu Chun; Dias Peter(a); Stampfl Jason(a); Tevelde Eric(a); Oania Robert(a); Tan Winny(a); Stampfl Chris(a); Lopez Carlos(a); Kumar Shant; Singh Sujay(a)
AUTHOR ADDRESS: (a)Imgenex, San Diego, CA, 92121**USA
JOURNAL: Molecular Biology of the Cell 10 (SUPPL.):p424a Nov., 1999
CONFERENCE/MEETING: 39th Annual Meeting of the American Society for Cell Biology Washington, D.C., USA December 11-15, 1999
SPONSOR: The American Society for Cell Biology
ISSN: 1059-1524
RECORD TYPE: Citation
LANGUAGE: English

2/3,AB/7 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12043477 BIOSIS NO.: 199900323996
IKKgamma mediates the interaction of cellular IkappaB kinases with the tax transforming protein of human T cell leukemia virus type 1.
AUTHOR: Chu Zhi-Liang; Shin Young-Ah; Yang Jin-Ming; DiDonato Joseph A; Ballard Dean W(a)
AUTHOR ADDRESS: (a)Howard Hughes Medical Inst., Vanderbilt University School of Medicine, 802 Rudolph Light Hall, N**USA
JOURNAL: Journal of Biological Chemistry 274 (22):p15297-15300 May 28, 1999
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The Tax oncoprotein of human T cell leukemia virus type 1 constitutively activates transcription factor NF-kappaB by a mechanism involving Tax-induced phosphorylation of IkappaBalpha, a labile cytoplasmic inhibitor of NF-kappaB. To trigger this signaling cascade, Tax associates stably with and persistently activates a cellular IkappaB kinase (IKK) containing both catalytic (IKKalpha and IKKbeta) and noncatalytic (IKKgamma) subunits. We now demonstrate that IKKalpha enables Tax to dock with the IKKbeta catalytic subunit, resulting in chronic IkappaB kinase activation. Mutations in either IKKgamma or Tax that prevent formation of these higher order Tax-IKK complexes also interfere with the ability of Tax to induce IKKbeta catalytic function in vivo. Deletion mapping studies indicate that amino acids 1-100 of IKKgamma are required for this Tax targeting function. Together, these findings identify IKKgamma as an adaptor protein that directs the stable formation of pathologic Tax-IKK complexes in virally infected T cells.

s ikb(w)alpha and kinase

```
            158  IKB
         835379  ALPHA
             54  IKB(W)ALPHA
         301153  KINASE
     S3      14  IKB(W)ALPHA AND KINASE
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...completed examining records
     S4      11  RD (unique items)
? t s4/3,ab/all
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4/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09593273 98369537

PKC-dependent modulation of **IkB alpha**-NFkB pathway in low metastatic B16F1 murine melanoma cells and in highly metastatic BL6 cells.

La Porta CA; Comolli R

Department of General Physiology and Biochemistry, University of Milan, Italy. Caterina.LaPorta@unimi.it

Anticancer research (GREECE) Jul-Aug 1998, 18 (4A) p2591-7, ISSN 0250-7005 Journal Code: 59L

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Protein **Kinase** C (PKC) is a family of at least 11 closely related isoforms with different modality of activation, and intracellular and tissue distribution. The aim of the present work was to analyse the effect of treatment with 0.1 microM TPA as well as treatment with specific inhibitors of individual PKC isoenzymes (Go6976 for c-PKC alpha and beta isoforms and BIM for c-PKCs and n-PKCs isoforms), on the NF-kB/**IkB alpha** pathway in the low and high metastatic B16F1 and BL6 murine melanoma cells. The DNA-binding activity of the transcription factors AP1, AP2, CREB and OTC was also considered. Different modality of activation for NF-kB and AP1 was demonstrated in the two cell lines with the possible specific involvement of c-PKCs isoforms. In fact, in the high metastatic BL6 cells the long-term treatment for 24 hours with TPA, with no c-PKC activation or the inhibition with Go6976 as well as with BIM, induced an increased NF-kB and AP1 DNA-binding activity. In contrast, in the low metastatic B16F1 cells the short-term treatment with TPA, induced the activation of c-PKCs isoforms, and enhanced NF-kB and AP1 DNA-binding activity. No significant changes were demonstrated for AP2, CREB and OTC DNA-binding activity in both cell lines.

4/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09529930 98300287

The DNA-dependent protein **kinase** participates in the activation of NF kappa B following DNA damage.

Basu S; Rosenzweig KR; Youmell M; Price BD

Joint Center for Radiation Therapy, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts 02115, USA.

Biochemical and biophysical research communications (UNITED STATES) Jun

9 1998, 247 (1) p79-8[illegible] ISSN 0006-291X Journal Code: 9Y8
Contract/Grant No.: [illegible]64585, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The NFkB transcription factor is activated by diverse stimuli, including Ionizing Radiation (IR) and the cytokine TNF alpha. The role of DNA-PK, a protein **kinase** involved in the response to DNA damage, in the activation of NF kappa B by IR and TNF alpha was examined. In M059K cells, which express DNA-PK, NF kappa B was activated by both TNF alpha and IR. In M059J cells, which do not express DNA-PK, IR did not activate NF kappa B, whereas TNF alpha induction of NF kappa B was still observed. In HeLa cells, wortmannin, an inhibitor of DNA-PK, blocked the induction of NF kappa B by IR but not by TNF alpha. DNA-PK also phosphorylated the NF kappa B inhibitory proteins **IkB-alpha** and IkB-beta in vitro, and deletion analysis demonstrated that DNA-PK phosphorylates 2 distinct regions of IkB-beta. These results indicate that DNA-PK participates in the activation of NF kappa B by IR but not by TNF alpha.

4/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08587937 96062284
Regulation of **IkB alpha** phosphorylation by PKC- and Ca(2+)-dependent signal transduction pathways.
Steffan NM; Bren GD; Frantz B; Tocci MJ; O'Neill EA; Paya CV
Department of Immunology, Mayo Clinic, Rochester, MN 55905, USA.
Journal of immunology (UNITED STATES) Nov 15 1995, 155 (10) p4685-91, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: RO1 AI36076-01, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE

The Ca(2+)-dependent phosphatase calcineurin, a target of FK506 and CsA, synergizes with PKC-induced activation of nuclear factor (NF)-kappa B in T cell lines. We have investigated whether this synergy is present in other cell types and the mechanism(s) by which these two pathways lead to NF-kappa B activation. While this synergy is present in other cell types, in the monocytic cell line U937 calcineurin is also sufficient to activate NF-kappa B. Having previously shown that Ca(2+)- and PKC-dependent pathways synergize by accelerating the degradation of **IkB alpha**, we focused on the regulation of **IkB alpha** phosphorylation. While PKC-dependent pathways sequentially result in the phosphorylation and in an incomplete degradation of **IkB alpha** in T cell lines, co-activation of Ca(2+)-dependent pathways accelerates the rate of **IkB alpha** phosphorylation and results in its complete degradation. Activation of Ca(2+)-dependent pathways alone do not result in the phosphorylation and/or degradation of **IkB alpha** in Jurkat T or in U937 cells. Treatment of T cells with the selective PKC inhibitor GF109203X abrogates the PMA-induced **IkB alpha** phosphorylation/degradation irrespective of activation of Ca(2+)-dependent pathways, but not the phosphorylation and degradation of **IkB alpha** induced by TNF-alpha, a PKC-independent stimulus. Contrary to the interaction with PKC, Ca(2+)-dependent pathways synergize with TNF-alpha not at the level of **IkB alpha** phosphorylation, but at the level of its degradation. These results indicate that Ca(2+)-dependent pathways, including the phosphatase calcineurin, participate in the regulation of NF-kappa B in a cell specific fashion and synergize with PKC-dependent and -independent pathways at the level of **IkB alpha** phosphorylation and degradation.

4/3,AB/4 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12432025 BIOSIS NO.: 200000185527
Transcription factor nuclear factor-kappa B is activated in neurons after focal cerebral ischemia.
AUTHOR: Stephenson Diane; Yin Tinggui; Smalstig E Barry; Hsu Mei Ann; Panetta Jill; Little Sheila; Clemens James(a)
AUTHOR ADDRESS: (a)Neuroscience Division, Eli Lilly and Company, 355 East Merrill Street, Dock 48, Indianapolis, IN, 46225**USA
JOURNAL: Journal of Cerebral Blood Flow and Metabolism 20 (3):p592-603 March, 2000
ISSN: 0271-678X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Nuclear factor-kappa B (NF-kappaB) is a multisubunit transcription factor that when activated induces the expression of genes encoding acute-phase proteins, cell adhesion molecules, cell surface receptors, and cytokines. NF-kappaB is composed of a variety of protein subunits of which p50-and p65-kappaDa (RelA) are the most widely studied. Under resting conditions, these subunits reside in the cytoplasm as an inactive complex bound by inhibitor proteins, IkappaBalpha and IkappaBbeta. On activation, IkappaB is phosphorylated by IkappaB **kinase** and ubiquitinated and degraded by the proteasome; simultaneously, the active heterodimer translocates to the nucleus where it can initiate gene transcription. In the periphery, NF-kappaB is involved in inflammation through stimulation of the production of inflammatory mediators. The role of NF-kappaB in the brain is unclear. In vitro, NF-kappaB activation can be either protective or deleterious. The role of NF-kappaB in ischemic neuronal cell death in vivo was investigated. Adult male rats were subjected to 2 hours of focal ischemia induced by middle cerebral artery occlusion (MCAO). At 2, 6, and 12 hours after reperfusion, the expression and transactivation of NF-kappaB in ischemic versus nonischemic cortex and striatum were determined by immunocytochemistry and by electrophoretic mobility gel-shift analysis. At all time points studied, p50 and p65 immunoreactivity was found exclusively in the nuclei of cortical and striatal neurons in the ischemic hemisphere. The contralateral nonischemic hemisphere showed no evidence of nuclear NF-kappaB immunoreactivity. Double immunofluorescence confirmed expression of p50 in nuclei of neurons. Increased NF-kappaB DNA-binding activity in nuclear extracts prepared from the ischemic hemisphere was further substantiated by electrophoretic mobility gel-shift analysis. Because the activation of NF-kappaB by many stimuli can be blocked by antioxidants in vitro, the effect of the antioxidant, LY341122, previously shown to be neuroprotective, on NF-kappaB activation in the MCAO model was evaluated. No significant activation of NF-kappaB was found by electrophoretic mobility gel-shift analysis in animals treated with LY341122. These results demonstrate that transient focal cerebral ischemia results in activation of NF-kappaB in neurons and supports previous observations that neuroprotective antioxidants may inhibit neuronal death by preventing the activation of NF-kappaB.

4/3,AB/5 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12113769 BIOSIS NO.: 199900408618
p75-mediated NF-kappaB activation enhances the survival response of developing sensory neurons to nerve growth factor.
AUTHOR: Hamanoue Makoto(a); Middleton Gayle; Wyatt Sean; Jaffray Ellis; Hay Ronald T; Davies Alun M
AUTHOR ADDRESS: (a)Department of Molecular Neurobiology, School of Medicine, Institute of DNA Medicine, Jikei Unive**Japan

JOURNAL: Molecular and Cellular Neuroscience 14 (1):p20-40 July, 1999
ISSN: 1044-7431
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We have investigated whether the transcription factor NF-kappaB plays a role in regulating neuronal survival by manipulating NF-kappaB activation in the nerve growth factor (NGF)-dependent sensory neurons of the embryonic mouse trigeminal ganglion. Overexpression of either the p65 or the p50 NF-kappaB subunits resulted in NF-kappaB activation and promoted in vitro survival as effectively as NGF. Expression of a superrepressor IkappaB-alpha protein prevented NF-kappaB activation in p65/p50-overexpressing neurons and caused the neurons to die as rapidly as NGF-deprived neurons. NGF treatment also activated NF-kappaB, and preventing this activation with superrepressor IkappaB-alpha reduced the NGF survival response. Antibodies that block binding of NGF to the p75 receptor prevented NGF-induced NF-kappaB activation and reduced the NGF survival response to the same extent as superrepressor IkappaB-alpha. Trigeminal neurons cultured from p65-/- embryos showed a reduced survival response to NGF compared with neurons from wild-type embryos and there was increased apoptosis of neurons in the trigeminal ganglia of p65-/- embryos in vivo. However, as with p75-deficient sensory neurons, p65-deficient sensory neurons showed a normal survival response to BDNF. These results reveal a role for NF-kappaB in regulating neuronal survival during embryonic development and suggest that in addition to the well-established Trk receptor tyrosine **kinase** signaling cascade, NGF enhances neuronal survival by signaling via a p75-mediated pathway.

4/3,AB/6 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11131996 BIOSIS NO.: 199799753141
Ionizing radiation and TNF-alpha stimulate gene expression of a Thr/Tyr-protein phosphatase HVH1 and inhibitory factor I-KAPPA-B-alpha in human squamous carcinoma cells.
AUTHOR: Kasid Usha(a); Wang Fun-Han; Whiteside Theresa L
AUTHOR ADDRESS: (a)E208, Research Build., Lombardi Cancer Cent., 3970 Reservoir Rd., N.W., Washington, DC 20007**USA
JOURNAL: Molecular and Cellular Biochemistry 173 (1-2):p193-197 1997
ISSN: 0300-8177
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Exposure of cells to ionizing radiation (IR) or tumor necrosis factor-alpha (TNF-alpha) results in the stimulation of the DNA binding activities of transcription factors, AP-1 and NF-kappa-B. HVHI/CL100, a dual specificity protein phosphatase, may attenuate the AP-1 response by dephosphorylating a key upstream element, mitogen-activated protein **kinase** (MAPK). The members of I-kappa-B family of proteins regulate the NF-kappa-B response. We examined the effects of IR and TNF-alpha on HVH1 and **IKB-alpha** gene expression. Our data demonstrate that IR or TNF-alpha treatment of head and neck squamous carcinoma cells (PCI-04A) increased the steady-state levels of HVH1 and I-kappa-B-alpha mRNAs; however, the induction patterns were different. TNF-alpha treatment led to a relatively prolonged stimulation of HVH1 and I-kappa-B-alpha mRNAs lasting at least 7 h, while IR caused a transient stimulation of these mRNAs and the expression returned to basal levels within 6 h post-IR treatment. Treatment of cells with cycloheximide did not prevent the IR or TNF-alpha-inducible expression of HVHI and I-kappa-B-alpha genes, indicating that these responses were independent of the new protein synthesis. These data imply that protein phosphatase

HVHI and regulatory factor I-kappa-B-alpha may play important roles in cellular response to IR and TNF-alpha. In addition, [redacted] kinetics of responsiveness indicates that the mechanisms of IR and TNF-alpha-induced signalling are distinct.

4/3,AB/7 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10409368 BIOSIS NO.: 199699030513
Casein **Kinase** II (CKII) phosphorylates **IKB-alpha** at S283, S289, S293, and T291 and is required for its degradation in vitro.
AUTHOR: McElhinny J A(a); Trushin S A; Bren G D; Chester N; Paya C V
AUTHOR ADDRESS: (a)Mayo Clinic, Rochester, MN 55905**USA
JOURNAL: FASEB Journal 10 (6):pA1119 1996
CONFERENCE/MEETING: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists New Orleans, Louisiana, USA June 2-6, 1996
ISSN: 0892-6638
RECORD TYPE: Citation
LANGUAGE: English

4/3,AB/8 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10321586 BIOSIS NO.: 199698776504
Inhibition of NF-kappa-b activation by a dominant-negative mutant of **IkB-alpha**.
AUTHOR: Chen Chao-Guang; Malliaros Jim; Katerelos Marina; D'Apice Anthony J F; Pearse Martin J
AUTHOR ADDRESS: Immunol. Res. Centre, St. Vincent's Hosp., Melbourne, VIC **Australia
JOURNAL: Molecular Immunology 33 (1):p57-61 1996
ISSN: 0161-5890
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The activity of the transcription factor NF-kappa-B is tightly regulated by the inhibitory molecule I-kappa-B-alpha. Upon stimulation, I-kappa-B-alpha is rapidly degraded and NF-kappa-B translocates to the nucleus to induce gene expression. The I-kappa-B-alpha degradation is preceded by phosphorylation, suggesting that this event plays a role in the activation of NF-kappa-B. In this study, we have mutated three potential phosphorylation sites in porcine I-kappa-B-alpha and found that expression of the Ser-32 mutant of I-kappa-B-alpha (I-S32A), but not Tyr-42 or Ser-262 mutants or wild-type I-kappa-B-alpha, blocked the activation of NF-kappa-B by TNF-alpha. These results suggest that the Ser-32 residue, a potential casein **kinase** II phosphorylation site, is critical for NF-kappa-B activation.

4/3,AB/9 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09395276 BIOSIS NO.: 199497403646
Double-stranded RNA-dependent protein **kinase** activates transcription factor NF-kappa-B by phosphorylating I-kappa-B.
AUTHOR: Kumar Aseem; Haque Jaharul; Lacoste Judith; Hiscott John; Williams Bryan R G(a)

AUTHOR ADDRESS: (a)Dep[redacted] Cancer Biol., Cleveland Clinic Foundation, 9500 Euclid Ave., Buildi[redacted]N1-06, Cleveland, OH**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 91 (14):p6288-6292 1994
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The induction of interferon (IFN) genes by viruses or double-stranded RNA (dsRNA) requires the assembly of a complex set of transcription factors on responsive DNA elements of IFN gene promoters. One of the factors necessary for regulating IFN-beta gene transcription is nuclear factor NF-kappa-B, the activation of which is triggered by dsRNA. It has previously been suggested that the dsRNA-activated p68 protein **kinase** (PKR) may act as an inducer-receptor, transducing the signal from dsRNA to NF-kappa-B through phosphorylation of the inhibitor I-kappa-B. We present direct evidence that PKR can phosphorylate I-kappa-B-alpha (MAD-3) and activate NF-kappa-B DNA binding activity in vitro. We further show that dsRNA induces an unusual phosphorylated form of **IKB-alpha**. The expression of a transdominant mutant PKR is able to perturb the dsRNA-mediated signaling pathway in vivo, suggesting a role for this **kinase** in IFN-beta gene induction.

4/3,AB/10 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09154695 BIOSIS NO.: 199497163065
Hypoxia causes the activation of NF-kappa-B and the phosphorylation of **IkB-alpha** at both tyrosine and serine residues.
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08973935 BIOSIS NO.: 199396125436
Rapid proteolysis of **IkB-alpha** is necessary for activation of transcription factor NF-kappa-b.
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ABSTRACT: Inducible gene expression in eukaryotes is mainly controlled by the activity of transcriptional activator proteins, such as NF-kappa-B (refs 1-3), a factor activated upon treatment of cells with phorbol

esters, lipopolysaccharide, interleukin-1 and tumour necrosis factor-alpha. Activation of NF-kappa-B involves release of the inhibitory subunit I-kappa-B from a cytoplasmic complex with the DNA-binding subunits Rel-A (formerly p65) and p50 (refs 6, 7). Cell-free experiments have suggested that protein **kinase** C and other kinases transfer phosphoryl groups onto I-kappa-B causing release of I-kappa-B and subsequent activation of NF-kappa-B. Here we report that I-kappa-B-alpha (formerly MAD-3) is degraded in cells after stimulation with phorbol ester, interleukin-1, lipopolysaccharide and tumour necrosis factor-alpha, an event coincident with the appearance of active NF-kappa-B. Treatment of cells with various protease inhibitors or an antioxidant completely prevented the inducible decay of I-kappa-B-alpha as well as the activation of NF-kappa-B. Our findings suggest that the activation of NF-kappa-B relies on an inducible degradation of I-kappa-B-alpha through a cytoplasmic, chymotrypsin-like protease. In intact cells, phosphorylation of I-kappa-B-alpha is apparently not